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(71) Applicant (for all designated States except US): **XENOPORT, INC.** [US/US]; 3410 Central Expressway, Santa Clara, California 95051 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **GALLOP, Mark A.** [NZ/US]; 511 Orange Avenue, Los Altos, California 94022 (US). **DAI, Xuedong** [CN/US]; 4305 Will Rogers Drive, San Jose, California 95129 (US). **SCHEUERMAN, Randall A.** [US/US]; 963 Sunlite Drive, Santa Clara, California 95050 (US). **RAILLARD, Stephen P.** [US/US]; 964 Trophy Drive, Mountain View, California 94040 (US). **MANTHATI, Suresh K.** [IN/US]; Apt. D102, 175 Calvert Drive, Cupertino, California 95014 (US). **YAO, Fenmei** [CN/US]; Apt. 7, 1920 California Street, Mountain View, California 94040 (US). **PHAN, Thu** [US/US]; 38190 Hastings Court, Fremont, California 94538 (US). **LUDWIKOW, Maria** [US/US]; 21122 Patriot Way, Cupertino, California 95014 (US). **PENG, Ge** [US/US]; 1002 Solana Drive, Mountain View, California 94043 (US). **BHAT, Seema** [IN/US]; 2444 Fairview Lane, Santa Clara, California 95051 (US).

(74) Agents: **PEASE, Ann M. Caviani et al.; DORSEY & WHITNEY LLP**, Suite 3400, Four Embarcadero Center, San Francisco, CA 94111 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,

PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

#### Declarations under Rule 4.17:

— as to the identity of the inventor (Rule 4.17(i)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(iii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE,

[Continued on next page]

(54) Title: SYNTHESIS OF ACYLOXYALKYL CARBAMATE PRODRUGS AND INTERMEDIATES THEREOF

(57) Abstract: Methods for synthesis of 1-(acyloxy)-alkyl carbamates, particularly, the synthesis of 1-(acyloxy)-alkyl carbamate prodrugs of primary or secondary amine containing drugs are described. Also described are methods for synthesis of 1-(acyloxy)-alkyl N-hydroxysuccinimidyl carbonates which are useful intermediates in the synthesis of 1-(acyloxy)-alkyl carbamates are also described.

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- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations
  - as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations

— of inventorship (Rule 4.17(iv)) for US only

**Published:**

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

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13 October 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

**A. CLASSIFICATION OF SUBJECT MATTER**  
 IPC 7 C07D207/40

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BEILSTEIN Data, WPI Data, CHEM ABS Data

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5 401 868 A (LUND ET AL) 28 March 1995 (1995-03-28) cited in the application Scheme A.	1-81
Y	----- WO 01/05813 A (ELI LILLY AND COMPANY; CHEN, SHU, HUI; RODRIGUEZ, MICHAEL, JOHN; SUN,) 25 January 2001 (2001-01-25) cited in the application Page 34: preparation of 1b-2. page 11, line 5 - page 12, line 2 ----- -/--	1-81

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

## \* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&amp;" document member of the same patent family

Date of the actual completion of the international search

17 June 2005

Date of mailing of the international search report

05.09.05

Name and mailing address of the ISA

 European Patent Office, P.B. 5818 Patentlaan 2  
 NL - 2280 HV Rijswijk  
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
 Fax: (+31-70) 340-3016

Authorized officer

Von Daacke, A

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	SUN, XICHENG ET AL: "Synthesis and evaluation of novel pseudomycin side-chain analogues. Part 3" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS , 11(23), 3055-3059 CODEN: BMCLE8; ISSN: 0960-894X, 2001, XP002332326 cited in the application examples 17a,17b -----	52-54
Y	SUN, XICHENG ET AL: "N-Acyloxymethyl carbamate linked prodrugs of pseudomycins are novel antifungal agents" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS , 11(14), 1875-1879 CODEN: BMCLE8; ISSN: 0960-894X, 2001, XP002332327 cited in the application examples 7-9 -----	52-54
E	WO 2005/019163 A (XENOPORT, INC; GALLOP, MARK, A; YAO, FENMEI; LUDWIKOW, MARIA, J; PHAN,) 3 March 2005 (2005-03-03) examples 78C,81C -----	53,55,56

# INTERNATIONAL SEARCH REPORT

international application no.  
PCT/US2004/043823

## Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
  
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
  
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
  
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-81

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-81

Method of synthesizing a compound (I) and single compounds (I).

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2. claims: 82-84

Method of synthesizing carbamates XI, XII and XIII using a compound of formula (I).

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Patent document cited in search report		Publication date	Patent family member(s)	Publication date
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			WO 2005019163 A2	03-03-2005
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